

14. (Amended) A composition comprising at least a first purified bioactive protamine in accordance with [any one of claims 1 through 13] claim 1.

17. (Amended) The composition of [any one of claims 14 through 16] claim 14, further comprising at least one additional biologically active agent.

18. (Amended) The composition of [any one of claims 14 through 17] claim 17, further comprising at least one additional coagulant.

19. (Amended) The composition of [any one of claims 14 through 18] claim 17, further comprising at least a first therapeutic protein or polypeptide.

22. (Amended) The composition of claim 20 [or 21], further comprising human insulin.

23. (Amended) The composition of [any one of claims 14 through 22] claim 14, wherein said composition is a pharmaceutical composition.

24. (Amended) The composition of [any one of claims 14 through 23, wherein said composition is an injectable pharmaceutical composition] claim 23, wherein said pharmaceutical composition is formulated for injection.

35. (Amended) A method of preparing at least a first [protamine that is] bioactive protamine, that has a low molecular weight and that has reduced immunoresponsiveness or toxicity compared to native protamine, comprising contacting a native protamine composition with at least a first proteolytic composition comprising an amount of at least a first proteolytic enzyme effective to produce said at least a first bioactive protamine.

37. (Amended) The method of claim 35 [or 36], wherein said at least a first proteolytic composition comprises at least a first ficin enzyme.

38. (Amended) The method of [any one of claims 35 through 37] claim 35, wherein said at least a first proteolytic composition comprises at least a first collagenase enzyme.

39. (Amended) The method of [any one of claims 35 through 38] claim 35, wherein said at least a first proteolytic composition comprises at least a first kallikrein enzyme.

40. (Amended) The method of [any one of claims 35 through 39] claim 35, wherein said at least a first proteolytic composition comprises at least a first proline-specific endopeptidase enzyme.

41. (Amended) The method of [any one of claims 35 through 40] claim 35, wherein said at least a first proteolytic composition comprises at least a first and at least a second proteolytic enzyme.

42. (Amended) The method of [any one of claims 35 through 41] claim 35, wherein said at least a first proteolytic enzyme is removed after said at least a first bioactive protamine is produced.

43. (Amended) The method of [any one of claims 35 through 42] claim 35, wherein at least a first and a second bioactive protamine is produced.

44. (Amended) The method of [any one of claims 35 through 43] claim 35, wherein a plurality of bioactive protamines are produced.

45. (Amended) The method of [any one of claims 35 through 44] claim 35, wherein the at least a first bioactive protamine produced has a molecular weight of between about 450 Daltons and about 1350 Daltons.

46. (Amended) The method of [any one of claims 35 through 45] claim 35, further comprising formulating the at least a first bioactive protamine produced in a pharmaceutically acceptable composition.

50. (Amended) The method of claim 48 [or 49], further comprising formulating the improved low molecular weight protamine species or fraction selected in a pharmaceutically acceptable composition.

52. (Amended) A kit comprising at least a first container that comprises at least a first purified bioactive protamine in accordance with [any one of claims 1 through 13 or at least a first composition in accordance with any one of claims 14 through 31, 47 or 51] claim 1.

53. (Amended) The kit of claim 52, further comprising at least [a second container that comprises at least] one additional anticoagulant.

55. (Amended) A method of inactivating heparin or low molecular weight heparin, comprising contacting heparin or low molecular weight heparin with a biologically effective amount of at least a first purified bioactive protamine in accordance with [any one of claims 1 through 13 or at least a first composition in accordance with any one of claims 14 through 31, 47 or 51] claim 1.

57. (Amended) A method of ameliorating an effect of heparin or low molecular weight heparin in a mammal, comprising administering to said mammal a therapeutically effective amount of at least a first pharmaceutical composition comprising at least a first purified bioactive protamine in accordance with [any one of claims 1 through 13 or at least a first composition in accordance with any one of claims 14 through 31, 47 or 51] claim 1.

58. (Amended) A method for treating or preventing undue or excessive bleeding in a mammal, comprising administering to a mammal having or at risk for developing excessive bleeding a therapeutically effective amount of at least a first pharmaceutical composition comprising at least a first purified bioactive protamine in accordance with [any one of claims 1

through 13 or at least a first composition in accordance with any one of claims 14 through 31, 47 or 51] claim 1.

59. (Amended) The method of [any one of claims 56 through 58] claim 58, wherein said mammal exhibits excessive bleeding associated with systemic heparinization.

60. (Amended) The method of [any one of claims 56 through 58] claim 58, wherein said mammal exhibits excessive bleeding associated with extracorporeal blood circulation.

61. (Amended) The method of [any one of claims 56 through 58] claim 58, wherein said mammal exhibits excessive bleeding associated with a disease or disorder.

62. (Amended) The method of [any one of claims 56 through 58] claim 58, wherein said mammal exhibits excessive bleeding associated with a trauma or surgery.

63. (Amended) The method of [any one of claims 56 through 62] claim 58, wherein at least a second coagulant is further administered to said mammal.

64. (Amended) A method of prolonging the bioavailability of insulin upon administration to a mammal, comprising co-administering insulin to a mammal in combination with an effective amount of a protamine composition that comprises at least a first purified bioactive protamine in accordance with [any one of claims 1 through 13 or at least a first composition in accordance with any one of claims 14 through 31, 47 or 51] claim 1.